- **Goals for management of osteoarthritis:**
  - **Relief of pain and suppression of inflammation.** This is achieved by:
    - Oral simple analgesics (paracetamol): when paracetamol is taken, it will either be conjugated with sulphate glucuronide (inactive metabolite) or oxidized to a reactive intermediate:
      - If it was taken at a therapeutic dosage, this reactive intermediate will be conjugated with glutathione to be converted to a glutathione conjugate and then to cysteine conjugate.
      - If it was taken at a higher dose (overdose), this will lead to liver damage.
        The maximum dose of paracetamol which can be taken daily is 4g.
    - **Topical NSAIDs:**
      - Methylsalicylate cream.
      - Diethylamine salicylate.
    - **Oral NSAIDs (they should be used at the lowest effective dose for the shortest possible period of time):**
      - Non-selective COX-1 inhibitors (in addition to COX-2). They cause adverse effects in the GI and renal systems (this is why these drugs must be prescribed with proton pump inhibitor).
      - Selective COX-2 inhibitors. These are contraindicated in patients with coronary artery disease and by-pass graft surgery.
    - **Opioid analgesics:**
      - **Tramadol**: synthetic opioid agonist.
      - **Co-proxamol**: dextropropoxyphene + paracetamol.
    - **Intra-articular corticosteroid injection:**
      - Triamcinolone acetate - Methylprednisolone acetate.
      - **They are indicated in case of:**
        - Severely inflamed single large joint with effusion.
        - When joint inflammation is unresponsive to NSAIDs.
        - When the patient can’t tolerate NSAIDs.
      - It should be done under aseptic technique to avoid introduction of joint infection.
      - Done up to 3 times/year to avoid systemic toxicity and joint damage (which can happen due to suppression of cartilage synthesis or relief of pain which may lead to overuse of the damaged joint).
      - Depot steroid preparation (slow-release preparations) are preferred for such purpose.
  - **Corticosteroids preparations can be:**
    - Non-ester (salt) preparations (water-soluble):
      - Quick onset of action.
      - Short duration of action.
      - Lower incidence of cutaneous adverse effects.
    - Ester preparations (water-insoluble: forming microcrystalline suspensions):
      - Slow onset of action.
      - Longer duration of action.
      - Higher incidence of cutaneous adverse effects.
  - **Adverse effects following corticosteroids injection:**
    - Capsular calcification: common (25-50%).
    - Flushing: relatively common (1-15%).
    - Post-injection flare: relatively common (1-10%).
  - **Contraindications to corticosteroid injections:**
    - Absolute: intra-articular sepsis, bacteremia, intra-articular fracture and joint instability.
- Maintaining the mobility (movement) and function of the inflamed joint. This is achieved by:
  ✓ Patient education.
  ✓ Physiotherapy.
  ✓ Joint replacement surgery.

- Local anesthetics:
  - Chemical structure:
    ✓ Aromatic lipophilic portion.
    ✓ Intermediate chain.
    ✓ Amine hydrophilic portion.

- Difference between esters and amides:

<table>
<thead>
<tr>
<th></th>
<th>Amino esters</th>
<th>Amino amides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotransformation</td>
<td>By plasma pseudocholinesterase</td>
<td>By liver (cytochrome P450) with renal excretion</td>
</tr>
<tr>
<td>Systemic toxicity</td>
<td>More likely in individuals with genetically-determined pseudocholinesterase deficiency</td>
<td>More likely to occur in patients with hepatic disease, reduction in hepatic blood flow and hepatic enzyme inhibitors</td>
</tr>
<tr>
<td>Hypersensitivity reactions</td>
<td>More likely (due to formation of PABA which is very antigenic)</td>
<td></td>
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</tbody>
</table>

- Systemic absorption of local anesthetics is affected by:
  ✓ Dosage.
  ✓ Pharmacological profile of drug employed (vasodilating properties).
  ✓ The presence of vasoconstrictor agent (such as adrenaline, noradrenaline and felypressin which is an analogue of vasopressin and safer to be given for patients with cardiovascular diseases in whom adrenaline is contraindicated). These agents are included in local anesthetic solution to:
    ✝ Retaining the local anesthetic in area injected.
    ✝ Reducing systemic toxicity by delaying its absorption into general circulation.
    ✝ Rendering the area of injection less hemorrhagic.
  ✓ Nature of administration site (vasularity of the tissues near the site of injection).
  ✓ Drug-tissue binding.

- Relative size and susceptibility of different types of nerve fibers to local anesthetics:
  ✓ Type B and type C nerve fibers (which have light or none myelination in addition to their small diameters) being more sensitive to block by local anesthetics.

- Methods of administration of local anesthetics:
  ✓ Surface anesthesia
  ✓ Infiltration anesthesia
  ✓ Intravenous regional anesthesia
  ✓ Nerve-block anesthesia
  ✓ Spinal anesthesia
  ✓ Epidural anesthesia
Summary of drugs used for local anesthesia:

<table>
<thead>
<tr>
<th>Subclass, Drug</th>
<th>Mechanism of Action</th>
<th>Effects</th>
<th>Clinical Applications</th>
<th>Pharmacokinetics, Toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AMIDES</strong></td>
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<tr>
<td>Lidocaine</td>
<td>Blockade of sodium channels</td>
<td>Slows, then blocks, action potential propagation</td>
<td>Short-duration procedures • topical (mucosal), intravenous, infiltration, spinal, epidural, minor and major peripheral blocks</td>
<td>Parenteral (e.g., peripheral block, but varies significantly based on specific site) • duration 1–2 h • 2–4 h with epinephrine • Toxicity: Central nervous system (CNS) excitation (high-volume blocks) and local neurotoxicity</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>Same as lidocaine</td>
<td>Same as lidocaine</td>
<td>Longer-duration procedures (but not used topically or intravenously)</td>
<td>Parenteral • duration 3–6 h • Toxicity: CNS excitation • cardiovascular collapse (high-volume blocks)</td>
</tr>
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</tr>
<tr>
<td><strong>ESTERS</strong></td>
<td></td>
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</tr>
<tr>
<td>Chloroprocaine</td>
<td>Like lidocaine</td>
<td>Like lidocaine</td>
<td>Very short procedures (not generally used topically or intravenously)</td>
<td>Parenteral • duration 30–60 min • 60–90 min with epinephrine • Toxicity: Like lidocaine</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Same as above • also has sympathomimetic effects</td>
<td>Same as above</td>
<td>Procedures requiring high surface activity and vasoconstriction</td>
<td>Topical or parenteral • duration 1–2 h • Toxicity: CNS excitation, convulsions, cardiac arrhythmias, hypertension, stroke</td>
</tr>
</tbody>
</table>

- Prilocaine, mepivacaine: Like lidocaine (but also risk of methemoglobinemia with prilocaine)
- Articaine: popular dental anesthetic
- Ropivacaine, levobupivacaine: Like bupivacaine
- Procaine: Like chloroprocaine (but not used epidurally)
- Tetracaine: Used primarily for spinal anesthesia; duration 2–3 h
- Benzocaine: used exclusively for topical anesthesia